

### **REMARKS**

Applicants thank the Examiner for the very thorough consideration given the present application. Claims 9-10 and 14-16 are currently pending in this application. Claims 11-12 have been cancelled. No new matter has been added by way of the present amendment. All of the amendments to the claims are merely editorial in nature to better conform the language of the claims to U.S. practice. Accordingly, no new matter has been added.

At the outset, the present application is believed to be in condition for allowance. Entry of the accompanying amendment is requested under 37 C.F.R. §1.116, as the amendment does not raise any new issues which would require further search and/or consideration by the Examiner. Furthermore, Applicants request entry of this amendment in order to place the claims in better form for consideration on Appeal.

In view of the amendments and remarks herein, Applicants respectfully request that the Examiner withdraw all outstanding rejections and allow the currently pending claims.

#### **Issues Under 35 U.S.C. §112, 1<sup>st</sup> paragraph**

Claims 11 and 12 stand rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. Applicants respectfully traverse.

Claims 11 and 12 have been cancelled by way of the present amendment. Accordingly, this rejection is moot.

Reconsideration and withdrawal of this rejection are thus respectfully requested.

**Obviousness-type double patenting rejections**

Claims 1 and 9-12 stand rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over the following issued patents and pending applications:

- Claims 1-15 of USP 6,297,261;
- Claims 1-13 of USP 6,696,475;
- Claims 12-20 of published application No. 2006/0058395; and
- Claims 21-39 of published application No. 2006/0160856.

Additionally, claims 11 and 12 stand rejected as being obvious over claims 1-41 of published application No. 2007/0293553. Applicants respectfully traverse.

Initially, Applicants note that claims 1 and 11-12 have been cancelled. Accordingly, the rejection of these claims is moot. Moreover, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Additionally, there must be a reason why one of ordinary skill in the art would modify the reference or combine reference teachings to obtain the invention. A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). There must be a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *Id.* The Supreme Court of the United States has recently held that the "teaching, suggestion, motivation test" is a valid test for

obviousness, albeit one which cannot be too rigidly applied. *Id.* Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *Id.*

The present invention is directed, *inter alia*, to a compound consisting of:

*N*-(3,5-Difluoro-phenyl)-*N'*-[3-(1*H*-tetrazol-5-yl)]-3'-trifluoromethyl-biphenyl-4-yl]-urea;

*N*-(3,5-Dichloro-phenyl)-*N'*-[3-(1*H*-tetrazol-5-yl)]-3'-trifluoromethyl-biphenyl-4-yl]-urea;

*N*-(3,5-Bis-trifluoromethyl-phenyl)-*N'*-[3-(1*H*-tetrazol-5-yl)]-3'-trifluoromethyl-biphenyl-4-yl]-urea; or a pharmaceutically acceptable salt thereof (emphasis added). The Examiner asserts that the presently claimed compounds are found in the genus and/or species claims such as in claim 3 of the '261 patent, and claim 6 of the '475 Patent. Applicants respectfully and strongly disagree, and submit that none of the cited references teach or suggest compounds comprising a 3-(1*H*-tetrazol-5-yl)- group as presently claimed. For this reason alone, this rejection is improper and should be withdrawn.

Moreover, Applicants have presented evidence of superior and unexpected properties exhibited by the claimed compounds (see Declaration under 37 C.F.R. 1.132 filed on November 17, 2008). The Examiner, however, indicates that the Declaration is unpersuasive, because (1) there was no side by side comparison between all of the compounds of the cited references, and (2) there was no explanation as to why the results of the  $K_D$  value of more than 100X lower than that of the prior art compounds is an unexpected result. Applicants respectfully disagree.

Initially, Applicants note that the Examiner's assertion that Applicants must compare the present invention to all of the compounds of the cited references is incorrect. Under U.S. patent

laws, Applicants only need to compare the closest prior art compound to the claimed compounds. Applicants submit that the closest prior art is WO 2004/022529, disclosing diarylurea derivatives and their use as chloride channel blockers. Applicants have submitted sufficient experimental data which compares the present application with the closest prior art. As such, Applicants have fulfilled their burden, and have clearly established superior and unexpected results.

Moreover, with regard to the Examiner's assertion that a  $K_D$  value of more than 100X lower than that of the prior art compounds is not an unexpected result, Applicants strongly disagree and submit that one skilled in the art would have expected similar compounds to have similar properties and activity. Thus, a 100X difference in  $K_D$  is clearly unexpected. As discussed in the Declaration of November 17, 2008, the compounds of the instant invention show a highly improved effect as blockers of VRAC (volume regulated anion channel), as compared to prior art compounds. This effect is evidenced by the much lower  $K_D$  value exhibited by the presently claimed compounds.

Because the invention, as set forth in Applicants' claims, is not disclosed or made obvious by the cited prior art, reconsideration and withdrawal of this rejection are respectfully requested.

### **Conclusion**

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn. It is believed that a

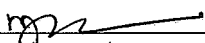
full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Vanessa Perez-Ramos, Reg. No. 61,158, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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